

### Amendments to the Specification

Please amend the paragraph beginning on page 1, line 5 of the instant application as follows.

This application is a continuation of U.S.S.N. 09/845,129, filed April 27, 2001, which is a continuation of U.S.S.N. 09/345,217, filed June 30, 1999 (now Patent No. 6,268,142), which is a continuation under 35 U.S.C. 111(a) and 37 CFR 1.53(b) of International ~~claims the benefit of Foreign~~ Application No. PCT/GB98/01481, filed May 21, 1998 which claims the benefit of ~~and~~ Foreign Application No. GB9711040.7, filed May 29, 1997; the entire contents of ~~each~~ which are hereby incorporated by reference.

Please amend the paragraph beginning on page 22, line 33 of the instant application as follows.

Appropriate probes may be designed to hybridize to a specific gene of the IL-1 locus, such as IL-1A, IL-1B or IL-1RN or a related gene. These genomic DNA sequences are shown in Figures 3, 4 and 5, respectively, and further correspond to SEQ ID Nos. 1, 2 and 3, respectively. Alternatively, these probes may incorporate other regions of the relevant genomic locus, including intergenic sequences. Indeed the IL-1 region of human chromosome 2 spans some 400,000 base pairs and, assuming an average of one single nucleotide polymorphism every 1,000 base pairs, includes some 400 SNPs loci alone. Yet other polymorphisms available for use with the immediate invention are obtainable from various public sources. For example, the human genome database collects intragenic SNPs, is searchable by sequence and currently contains approximately 2,700 entries (<http://hgbase.interactiva.de>). Also available is a human polymorphism database maintained by the Massachusetts Institute of Technology (MIT SNP database (<http://www.genome.wi.mit.edu/SNP/human/index.html>)). From such sources SNPs as well as other human polymorphisms may be found.

Please amend the paragraph beginning on page 32, line 1 of the instant application as follows.

The design of additional oligonucleotides for use in the amplification and detection of IL-1 polymorphic alleles by the method of the invention is facilitated by the availability of both updated sequence information from human chromosome 2q13 - which contains the human IL-1

locus, and updated human polymorphism information available for this locus. For example, the DNA sequence for the IL-1A, IL-1B and IL-1RN is shown in Figures [[1]] 3 (GenBank Accession No. X03833), [[2]] 4 (GenBank Accession No. X04500) and [[3]] 5 (GenBank Accession No. X64532) respectively. Suitable primers for the detection of a human polymorphism in these genes can be readily designed using this sequence information and standard techniques known in the art for the design and optimization of primers sequences. Optimal design of such primer sequences can be achieved, for example, by the use of commercially available primer selection programs such as Primer 2.1, Primer 3 or GeneFisher (See also, Nicklin M.H.J., Weith A. Duff G.W., "A Physical Map of the Region Encompassing the Human Interleukin-1 $\alpha$ , interleukin-1 $\beta$ , and Interleukin-1 Receptor Antagonist Genes" Genomics 19: 382 (1995); Nothwang H.G., et al. "Molecular Cloning of the Interleukin-1 gene Cluster: Construction of an Integrated YAC/PAC Contig and a partial transcriptional Map in the Region of Chromosome 2q13" Genomics 41: 370 (1997); Clark, et al. (1986) Nucl. Acids. Res., 14:7897-7914 [published erratum appears in Nucleic Acids Res., 15:868 (1987) and the Genome Database (GDB) project at the URL <http://www.gdb.org>).